Sensitivity Analysis of the Bone Fracture Risk Model

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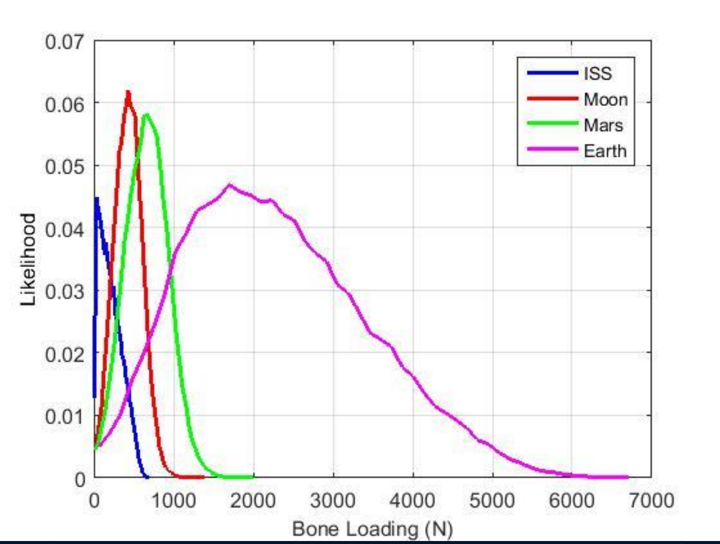
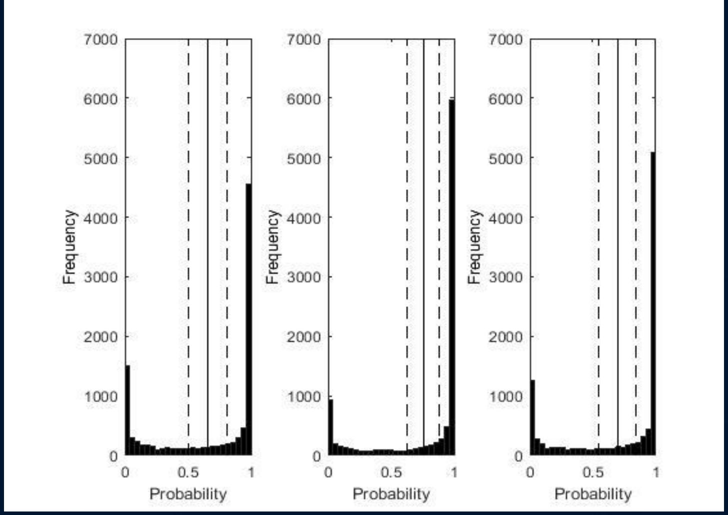
Introduction

- The probability of astronaut bone fracture before, during and after spaceflight is quantified with the NASA Bone Fracture Risk Module (BFxRM)*
- The BFxRM uses a probabilistic modeling approach with distributions of model parameters which introduce uncertainty into the probability results
- This uncertainty masks the ability to quantify the effect of countermeasures on fracture probability



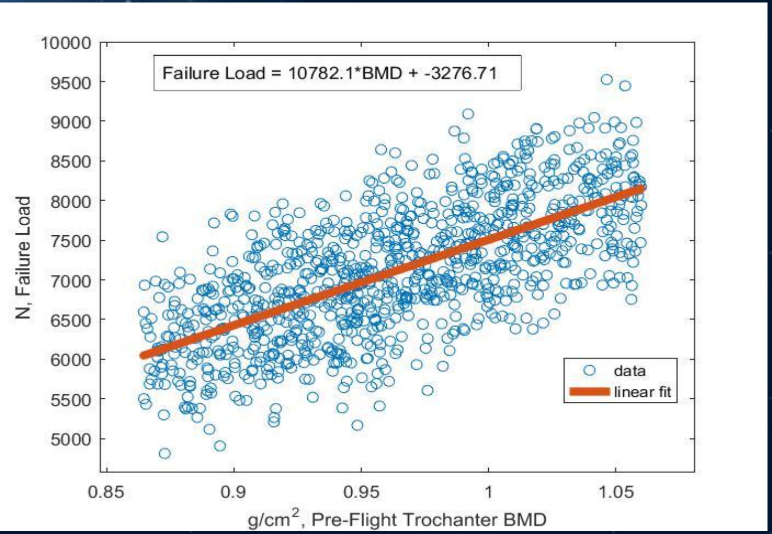


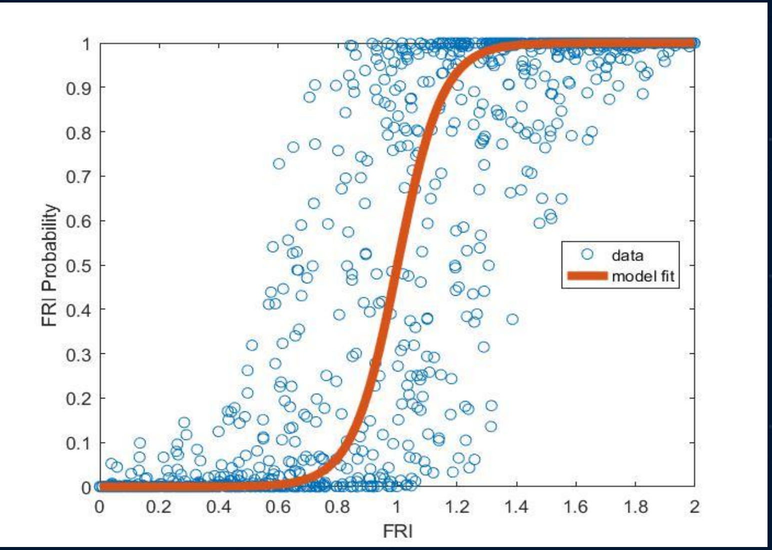
* Nelson et al., "Development and validation of a predictive bone fracture risk model for astronauts," *Ann. Biomed. Eng.*, 37(11), 2337–59, 2009.

Introduction

- We hypothesize that the large uncertainty is due to the inability to measure key contributors to bone strength with areal bone mineral density (aBMD) techniques*

- This presentation reports the results of a sensitivity analysis of the BFxRM in order to identify the parameters which contribute the most to the uncertainty





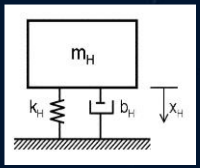
* Zysset et al., "Clinical Use of Quantitative Computed Tomography-Based Finite Element Analysis of the Hip and Spine in the Management of Osteoporosis in Adults: The 2015 ISCD Official Positions-Part II," *J. Clin. Densitom.*, 18(3), 359–92, 2015.

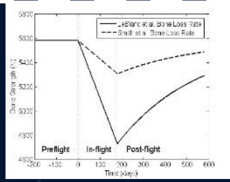
BFxRM Model Components

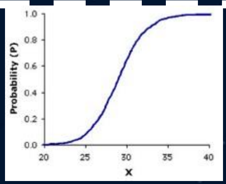
- A biomechanical model to estimate applied loads from a loading event
- An algorithm for spaceflight bone mineral density (BMD) loss and a mathematical relationship between BMD and bone strength
- The fracture risk index (FRI) which is the ratio of applied load to bone strength
- An algorithm to convert FRI to bone fracture probability

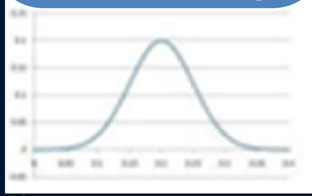
Monte Carlo Simulation

Probability and magnitude of loading event → **Estimate relative skeletal strength** → **Est. fx probability by load to strength ratio** → **Most likely probability of fracture for event + uncertainty**



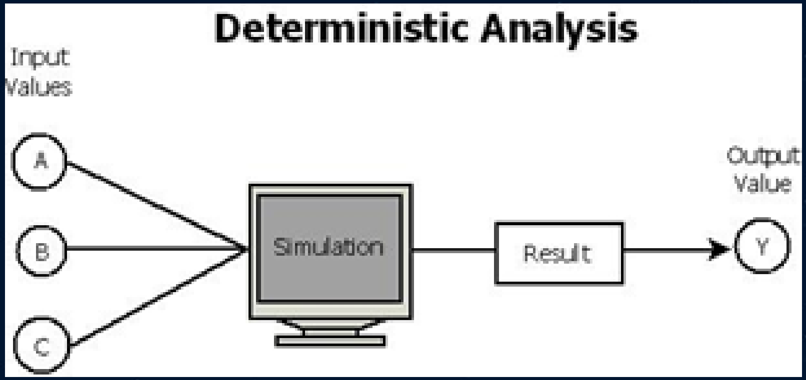


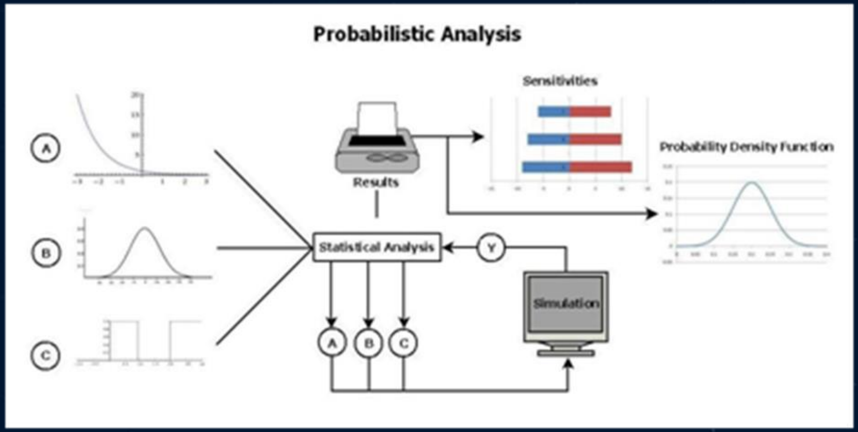




BFxRM Model Parameters

- Environmental factors
  - Gravity level
  - EVA suit/no EVA suit
- Factors associated with the fall event
  - Fall height
  - Translational velocity
  - Attenuation
- Mass and anthropometric values of the astronaut
  - Body mass
  - Effective hip mass
  - Hip spring and damping characteristics
- BMD characteristics
  - Preflight BMD value
  - Rate of BMD loss during spaceflight
  - Maximum BMD loss
  - Recovery half-life
- Characteristics of the relationship between BMD and bone strength
  - Slope of the relationship
  - Intercept of the relationship
- Bone fracture characteristics
  - Parameters associated with the conversion between FRI and fracture probability





Sensitivity Analysis

- Performed to determine which parameters cause the most variation in model results
- Fracture probability for pre-flight, 0 days post-flight and 365 days post-flight is calculated 100,000 times as the parameter distributions are sampled
- A correlation coefficient is found between the sample set of each model parameter and the calculated fracture probabilities
- Each parameter's contribution to the variance is found by:
  - Squaring the correlation coefficients
  - Dividing by the sum of the squared correlation coefficients
  - Multiplying by 100%

Results

- The top five most sensitive parameters:

	Preflight	0 days Post-flight	365 days Post-flight
Parameters	% Variance	% Variance	% Variance
Hip Spring Constant (k_H)	36.7	37.7	37.4
Probability Equation Midpoint FRI Value (μ)	35.5	29.0	33.4
Preflight Trochanter BMD (BMD_{Pre})	19.9	21.7	20.6
Trochanter Bone Strength Equation Intercept (B_{BS})	4.56	5.16	4.7
Effective Hip Mass Multiplier (h_m)	1.65	1.50	1.58

Future Work

- Updates to the BFxRM are planned
  - Update the applied load model with any additional hip spring and damping constant information from new journal articles
  - Perform a Baysian update to the BMD to bone strength relationship using FEM bone strength data
  - Update the relationship between FRI and fracture probability with data sets that include fracture outcomes
  - Identify additional validation tests that can be performed and update the NASA-STD-7009A compliance matrix for the BFxRM

Thank you

Questions?